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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/125,635	08/21/1998	PAUL MELTZER	4239-50420	8012

7590 08/27/2002

KLARQUIST SPARKMAN CAMPBELL
LEIGH & WHINSTON
ONE WORLD TRADE CENTER
121 SW SALMON STREET SUITE 1600
PORTLAND, OR 972042988

EXAMINER	
BASI, NIRMAL SINGH	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 08/27/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/125,635	Applicant(s) Meltzer et al
	Examiner Nirmal S. Basi	Art Unit 1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Nov 15, 2001*.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *12-69* is/are pending in the application.

4a) Of the above, claim(s) *21-54* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *12-20 and 55-69* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Response filed 11/15/01 (paper number 18) has been entered. Response filed 8/27/01 (paper number 16) has been entered. Response filed 6/11/01 (paper number 14) has been entered.

2. ***Election/Restriction***

The declaration of Jeffrey Trent and Paul Metlzer has been fully considered and found persuasive. The claims of Group II (polypeptide encoded by Group I) and Group IV (method of identifying a candidate compound which inhibits estrogen (ER) receptor-dependent transcription comprising contacting the compound with the AIBI polypeptide of claim 12 is rejoined. The claimed rejoined include the product, method of making the product (none is claimed) and first method of use of the product. Therefore Group I (polynucleotide of claims 55-65), Group II (polypeptide of claims 12-13) and Group IV (claims 14-20 drawn to method of identifying a candidate compound which inhibits estrogen receptor (ER) dependent transcription comprising contacting the compound of with the A1B1 polypeptide of claim 12) will be examined. Newly added claims 66-67 pertaining to polypeptide and claims 68-69 pertaining to polynucleotide will also be examined.

3. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claims 66-69 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 66-69 recite polynucleotide and polypeptide sequences but do not recite that they are isolated or purified. Claims 65 recites host cell comprising DNA of claim 55 but do not recite that the cells are isolated or purified. The claims as currently recited encompass these naturally-occurring compounds or cells. Therefore, the compounds and cells as claimed are a product that occurs in nature and does not show the hand of man, and as such is non-statutory subject matter. It is suggested that the claims be amended to recite "an isolated and purified" to overcome this rejection.

Claim Rejection, 35 U.S.C. 112

4. Claims 12-13, 14-20, 55-65 and 66-69 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 12, 13, 19, 20, 55, 66 and 67 are indefinite because it is not clear what are "conservative variants thereof". "Conservative variants thereof" does not provide any structural limitation on the claim and the metes and bounds of the claim cannot be determined.

Claim 12 is indefinite because it is not clear when a polypeptide is substantially pure as when it is not substantially pure so as to allow the metes and bounds of the claim to be determined. Similarly claim 55 is indefinite for the use of substantially

Claims 61 is indefinite because "high stringency" hybridization condition are not disclosed. The metes and bounds of the group of sequences that would meet the limitations of the claim depend upon the precise conditions under which hybridizations were performed including wash conditions.

Claim 14 is indefinite because the method steps do not achieve the goal of identifying a candidate compound which inhibits estrogen receptor-dependent transcription. An acceptable method claim must contain three sections: 1) a preamble, 2) method steps that clearly define what is to be done in each step, and 3) a conclusion that what was stated in the preamble was achieved. It is not clear how the binding of compound with A1B1 polypeptide indicates that the compound inhibits ER-dependent transcription, since no transcription is measured. Similarly, in claim 18 is indefinite because the method steps do not achieve the goal of identifying a candidate compound which inhibits estrogen receptor-dependent transcription.

Claim 15 is indefinite because it is not clear what is an Per/Arnt/Sim(PAS) domain as to allow the metes and bounds of the claims to be determined. The term Per/Arnt/Sim (PAS) domain does not provide a structural limitation. It is suggested said domain be identified by SEQ ID NO: to overcome the rejection. Similarly claim 19 is indefinite because it is not clear what is a PAS domain and claim 20 is indefinite because it is not clear what is a bHLH domain.

Claim 16 is indefinite because it is not clear what is a basic helix-loop-helix (bHLH) domain as to allow the metes and bounds of the claims to be determined. The term basic helix-loop-helix (bHLH) domain does not provide a structural limitation. It is suggested said domain be identified by SEQ ID NO: to overcome the rejection.

Claims 17 and 18 are indefinite because it is not clear what is the ER polypeptide or ER dependent transcription as to allow the metes and bounds of the claims to be determined.

Claims 56-60 and 62-65 are rejected for depending on an indefinite base claim and fail to resolve the issues raised above.

Claim Rejection, 35 U.S.C. 112, first paragraph

5. Claims 12-20, 55-56, 58-69 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to polypeptide:

a) comprising SEQ ID NO:8 or conservative variant thereof, wherein the polypeptide acts as a co-activator of a steroid hormone receptor,

b) comprising SEQ ID NO:4 or conservative variant thereof, wherein the polypeptide acts as a co-activator of a steroid hormone receptor.

c) polypeptide comprising SEQ ID NO:2 or SEQ ID NO:3 or conservative variants thereof

The claims are drawn to polynucleotide:

a) encoding the polypeptide comprising SEQ ID NO:8 or conservative variants thereof, wherein the polypeptide acts as co-activator of a steroid hormone receptor, further where the polypeptide comprises SEQ ID NO:4, 2, 3

b) encoding the A1B1 polypeptide which hybridizes to the DNA having the sequence of SEQ ID NO:1, or a complement thereof, wherein the polynucleotide has at least 90% identity to SEQ ID NO:1

c) polynucleotide having at least 75% or 90% homology to SEQ ID NO:1 wherein the encodes a polypeptide that acts as co-activator of a steroid hormone receptor

The claims are further directed to cell comprising the DNA encoding the human A1B1 polypeptide. Claims 14-20 are directed to use of the above mentioned polypeptides.

The claims, as written, encompass polynucleotides, polypeptides which vary substantially in length and also in nucleotide composition. The instant disclosure of a polynucleotide of SEQ ID NO:1 encoding the polypeptide of SEQ ID NO:4 does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera including full-length genes, nucleic acids encoding chimeric proteins or fusion proteins, variants, fusion proteins, chimeric proteins.. A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, proteins defined by nucleotide or amino acid sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the claimed genus of polynucleotides. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. The

specification proposes to discover other members of the genus by using hybridization (pages 7). There is no description, however, of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polynucleotides encompassed. No identifying characteristic or property of the instant polynucleotides is provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of specific nucleotide sequences and the inability to screen, is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed. The inclusion of the language "acts as a coactivator of a steroid hormone receptor does not overcome the rejection of record. There is no disclosure that the polynucleotide of SEQ ID NO:1 encodes a the polypeptide (SEQ ID NO:4) that can act as a coactivator with all steroid hormones.

Accordingly, the specification does not provide a written description of the polynucleotides, polypeptides of the invention and the methods of their use.

Claim Rejection, 35 U.S.C. 112

6. Claims 12-20, 55-56, 58-69 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a) an isolated DNA comprising a nucleotide sequence encoding a polypeptide that binds estrogen receptor, wherein the polypeptide comprises SEQ ID NO: 4, b) isolated DNA comprising a nucleotide sequence encoding a polypeptide that binds estrogen receptor, wherein the polypeptide is encoded by the nucleic acid of SEQ ID NO:1 c) degenerate variants of an isolated DNA comprising a nucleotide sequence encoding a polypeptide that binds estrogen receptor , wherein the polypeptide comprises SEQ ID NO: 4, d) the complement of the DNA stated in a) and b), e) specific fragments of the DNA of SEQ ID NO:1 which are of sufficient length to be used for nucleic acid hybridization probes (ie. specifically bind to the complement of the DNA of SEQ ID NO:1), f) specific fragments of the DNA of a)-c) which encode fragments of the polypeptide of SEQ ID NO:4, said fragments being useful for expression of epitopic portions of the polypeptide of SEQ ID NO:4, wherein said epitopic portions are useful for producing antibodies which specifically bind to the protein of SEQ ID NO:4, g) specific fragments of the polypeptide that binds estrogen receptor, wherein the polypeptide consists SEQ ID NO: 4, h) vectors comprising the said DNA and host cell transformed with said DNA, polypeptide encoded by said DNA, and I) a process of identifying candidate compounds that inhibit estrogen receptor-dependent transcription by using the above mentioned polypeptides and polynucleotides, does not reasonably provide enablement for other DNA, polypeptides, vectors, cells or methods of use of

other polynucleotides or polypeptides. The, specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification disclose the polynucleotide of SEQ ID NO:1 encodes a protein (SEQ ID NO:4) that binds estrogen receptor. The claims encompass the binding of the claimed protein to all steroid hormones. The claims further encompass conservative variants. The variants carry no patentable weight and read on unrelated molecules. Further the hybridization conditions are not specific and will result in the isolation of unrelated or inactive molecules. Also claims with per cent identity read on unrelated molecule. The critical feature of the invention is not disclosed, nor how it is related to function. Applicant has not disclosed how to make active molecules that bind the scope of the steroid hormones claimed. The critical feature of the isolated DNA of SEQ ID NO:1 is that it encodes a polypeptide that binds estrogen receptor. The scope of the claims encompass other fragments that have not been specifically disclosed to have the critical feature of the invention, and further lack the elements that have been disclosed enabling above. Without disclosure of where specially, in the structure of the molecule, the critical feature is contained it accordingly follows that the specification does not adequately teach how to make or use a commensurate number of such species. One cannot make or use that which cannot be envisioned. Further using claimed DNA fragments, lacking the critical feature, for hybridization may lead to binding to nucleic acids which encode polypeptides unrelated to the protein of SEQ ID NO: 4. Applicant has not disclosed how to use said DNA. Further, while the person of ordinary skill in the art would, in light of the

specification be able to make hybridization probes using fragments of SEQ. ID. NO:1, or alternatively would be able to use SEQ. ID. NO:1 or degenerate variants thereof or fragments of either to produce epitopic fragments of the protein of SEQ. ID. NO:4, the scope of the claims, which encompass any nucleic acid encoding any fragment, part or derivative that binds any steroid hormone receptor, which encompasses variant thereof, is simply not enabled by the disclosure. The disclosure does not teach how to make such fragments, or to use any of the numerous fragments which did not share one of the two functions set forth above e.g. use as a hybridization probe, or for the production of an epitope fragment of protein of SEQ. ID. NO:4. In addition, because of degeneracy of the genetic code the specification does not teach how to use many of the polynucleotide sequences that would not specifically hybridize to the polynucleotide of SEQ ID NO:1. It is noted that numerous such sequences would not hybridize to the nucleic acids encoding the protein of SEQ. ID. NO:4, nor would they themselves encode a protein that binds a steroid hormone receptor. Due to the large quantity of experimentation necessary to identify the DNA of instant invention containing the critical feature of the invention, the lack of direction/guidance presented in the specification regarding the identification, purification, isolation and characterization of said DNA, the unpredictability of the effects of mutation on the structure and function of proteins (since mutations of the DNA encoding the protein of SEQ ID NO:4 are also encompassed by the claim), and the breadth of the claim which fail to recite sufficient structural limitations, undue experimentation would be required of the skilled artisan to make or use the claimed invention in its full scope.

Further pertaining to claims 61, the instant fact pattern closely resembles that in Ex parte Maizel, 27 USPQ2d 1662 (BPAI 1992). In Ex parte Maizel, the claimed invention was directed to compounds which were defined in terms of function rather than sequence (i.e., "biologically functional equivalents"). The only disclosed compound in both the instant case and in Ex parte Maizel was the full length, naturally occurring protein. The Board found that there was no reasonable correlation between the scope of exclusive right desired by Appellant and the scope of enablement set forth in the patent application. Even though Appellant in Ex parte Maizel urged that the biologically functional equivalents would consist of proteins having amino acid substitutions wherein the substituted amino acids have similar hydrophobicity and charge characteristics such that the substitutions are "conservative" and do not modify the basic functional equivalents of the protein, the Board found that the specification did not support such a definition, and that the claims encompassed an unduly broad number of compounds. Such is the instant situation. Clearly, a single disclosed sequence does not support claims to any DNA derived from the same, given the lack of guidance regarding the structure of the nucleotide sequence. Likewise, expression vectors, comprising claimed DNA, cell transformed with said DNA and process for producing protein using said cell are not enabled for these reasons given above.

No claim is allowed

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal Basi whose telephone number is (703) 308-9435. The examiner can normally be reached on Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for this Group is (703) 308-0294.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Nirmal S. Basi
Art Unit 1646
August 26, 2002

Michael D. Pak
MICHAEL PAK
PRIMARY EXAMINER